

AN ADENOMA OF SEBACEOUS GLANDS OF THE ABDOMINAL WALL.¹

WITH A REVIEW OF THE LITERATURE OF ADENOMA AND HYPERPLASIA OF THE SEBACEOUS GLANDS.

BY WILLIAM COGSWELL CLARKE, M.D.,
OF NEW YORK.

THIS tumor is of surgical and pathological interest both from its extreme rarity and from the difficulty of diagnosis. Dr. Emil Bock, in 1880, probably gave the first good description of a real adenoma of sebaceous glands, accompanied by drawings of microscopic sections. Many writers have described hyperplasia of the glands and also primary lesions of the skin where the glands have become secondarily involved, and called them "Adenomata Sebacea." But if one takes into consideration the classification of Unna, which is quoted in the latter part of this article, the difference is manifest.

Present Case.—In July, 1903, a Jewess, eleven years of age, was referred from the Medical to the Surgical Class of the Out-Patient Department of the Roosevelt Hospital, for the removal of a tumor of the abdominal wall.

Past History.—She had always been in good health and had never received an injury of any kind. Menstruation had not commenced, although pubic and axillary hair was fully grown and her breasts were well developed.

Present History.—Three years ago she noticed in the skin a tumor about the size of a pea, situated three centimetres above and five centimetres to the left of the umbilicus. It lay in a line drawn from the nipple downward and slightly inward. Both she and her mother were positive that the growth had not always been present, and also that from the time of its first appearance it had

¹ A study from the Department of Pathology of the College of Physicians and Surgeons (Columbia University), New York.

slowly increased in size, at the same time becoming dark in color. Three months ago it suddenly began to grow more rapidly. There had never been any pain or unpleasant sensation connected with it, and she had not lost flesh or strength.

Physical Examination.—Inspection. The patient was well nourished, apparently in perfect health, large and strong for her years. No growths were seen on any other part of the body. The tumor was oval, smooth, and prominent, about six centimetres by five centimetres in diameter, bulging forward three centimetres. There was some wrinkling of the skin at the angle where it turned to pass over the tumor. On the dome of the growth for an area of three centimetres, the skin was thin, smooth, and dark, on account of the presence of many enlarged blood-vessels.

Palpation.—The tumor was a soft, fluctuating mass apparently made up of two cysts, one considerably larger than the other. It was intimately adherent to the deeper layers of the skin. The superficial layers of the latter were movable over the growth, showing not even the slightest point of attachment. The growth was freely movable on the deeper parts; the abdominal muscles put upon the stretch did not at all limit its mobility.

Operation.—Ether anæsthesia. An elliptical incision surrounding the tumor and exposing its base allowed an easy dissection of the tumor from its bed in the fat of the subcutaneous tissue of the abdominal wall. After its removal, a certain amount of fat and subcutaneous tissue still remained undisturbed, overlying the abdominal muscles. The wound was readily closed by three deep catgut sutures, and by black silk for the skin. The wound healed by primary union and the sutures were removed on the eighth day.

Morphological Examination.—Macroscopic. The material consisted of seven cysts, which composed about four-fifths of the tumor, and the balance was an irregular wedge-shaped mass of firm tissue situated between the two largest cysts. The average size of the cysts was about two centimetres in diameter,—the largest, four centimetres; the smallest, three millimetres. Five of these cysts contained a thin, watery, dark-brown fluid, while the smallest (Plate I, P) was filled with a dark, firm, sebaceous material. The true skin was not attached to the surface of any of the cysts, although the mass was indirectly adherent to the skin because of its situation in the subcutaneous connective tissue.

Microscopic Examination.—Two-fifths of the firm tissue was stroma and the balance epithelial masses and small cysts. The stroma consisted of rather dense connective tissue in bands, whose fibres were arranged in parallel rows. These bands ran between the epithelial alveoli and at times in the alveoli, acting as trabeculæ. In places, the connective-tissue bands, especially some of the connective-tissue trabeculæ found in the alveoli, had undergone hyalin degeneration. Blood-vessels were scanty throughout the stroma. The adventitia of the vessel walls was somewhat thickened. The endothelial cells of the intima were markedly swollen and in places increased in number. Sweat-glands were present, and both the stroma and epithelium were normal in appearance.

Epithelial Cells.—The epithelial cells were arranged in cylinders and oval masses, sections of which in places were much elongated, in others, round or oval (Plates I and II). The width of the alveoli on an average ran from 75 to 800 microns, the majority being about 500 microns. The cells in the alveoli were arranged for the most part in a number of small nests, each consisting of from twenty to thirty cells, concentrically placed. Towards the outside of an alveolus the cells were arranged in rows parallel to its boundary. This regular arrangement of cells was especially marked in the outermost row. It is worthy of note that in no instance was there an extension of the epithelial cells into the stroma itself, but they were massed together and surrounded by a firm band of connective tissue. The cells themselves were of large size, cuboidal, polyhedral, columnar, or even in places cylindrical in shape. The most regular and symmetrical measured from thirty to thirty-five micromillimetres in diameter. The cell-body stained easily with eosin, taking on a fairly deep color, and appeared faintly granular. The nucleus was large and oval, occupying about one-third of the cell-body. It stained very readily with hæmatoxylin, showing many rather coarse, deeply stained granules. A nucleolus was seen in each nucleus. No mitotic figures were observed in the cells of any of the sections. Spine or so-called "prickle cells" could not be found.

Cell Degeneration.—Scattered here and there, usually towards the centre of the alveoli, or else in the epithelial layers of the cyst walls, were many isolated cells which stained deep purple, both with hæmatoxylin-eosin and picro-acid-fuchsin (Plate III, A).

PLATE I.

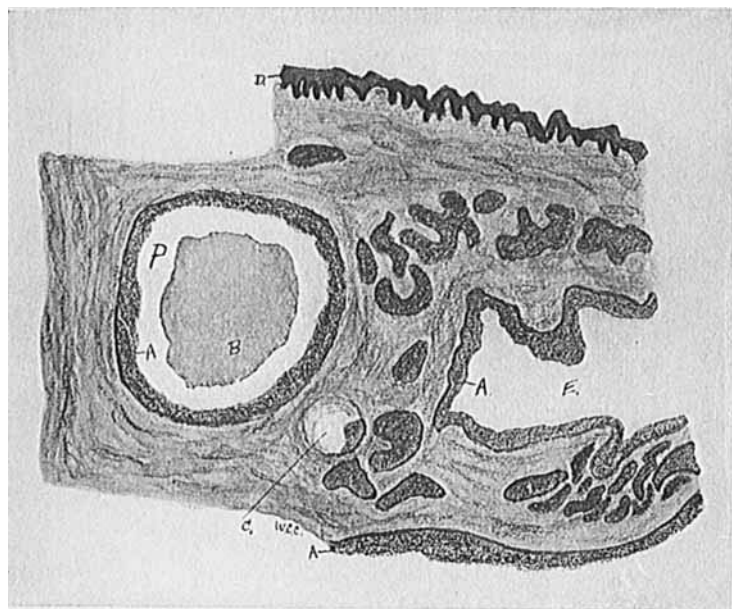


PLATE II.

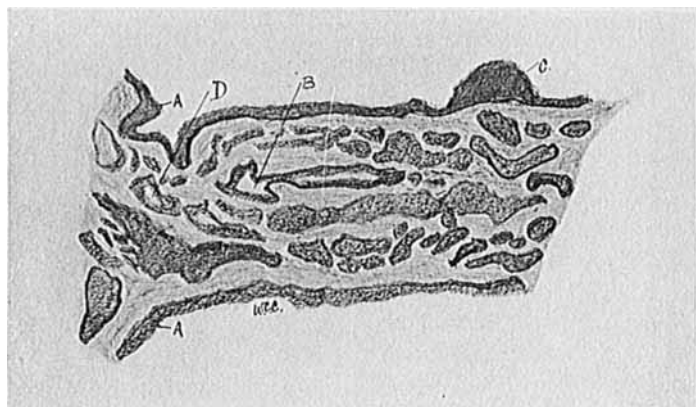
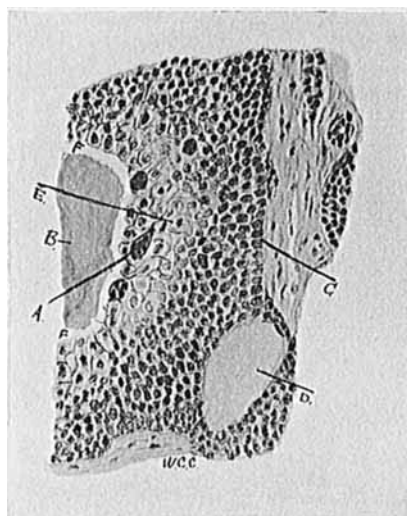


PLATE III.



The cell-bodies, staining purple, were often elongated, either homogeneous or vacuolated, with no nuclei showing; apparently mucous degeneration of the epithelial cells. Besides the above cells, some alveoli contained an area whose cells were large, measuring forty-three micromillimetres in diameter, and vesicular in shape. The cell-body did not stain with either hæmatoxylin-eosin or picro-acid-fuchsin. It was occupied by fine vacuoles, very regular in shape. Occasionally larger vacuoles were seen. The cell-wall was thin, sharply outlined, at times broken down as though the cells had ruptured. This condition was most often observed towards the centre of the alveoli. The nucleus was round and measured eight and six-tenths micromillimetres in diameter. It was situated in some near the centre of the cell, in others near the cell-wall. After staining, the color of the nucleus was a rather faint homogeneous blue, not granular (Plate IV, A).

Cysts—Walls and Contents.—In addition to the seven cysts whose gross appearance has already been described, many others were noted in the microscopic examination, measuring from 160 to 640 microns in diameter. They were for the most part round, at times oval, or very much elongated. The walls of the cysts varied considerably. At times, when the cyst was situated in the centre of an alveolus, the limiting walls were sharp and clean-cut, and the epithelial cells were even and regular in shape, no degenerated or ruptured cells appearing (Plate II, D). Again, especially in the larger cysts, the walls were made up of fifteen to twenty-five layers of epithelial cells, the innermost of them being broken and disintegrated (Plate I and Plate II at A, A, A, A). Here and there appeared the cells mentioned above as undergoing mucous degeneration. Some of the small cysts also had uneven walls, a few of them bounded by the large, clear staining cells undergoing fatty metamorphosis (Plate IV, C), others by jagged walls in which were many cells undergoing mucous degeneration (Plate III, F, F). The contents of some of the smaller cysts, when not dissolved while fixing and hardening the specimen, stained a deep purple color, and invariably there were noted in the walls cells which were undergoing the so-called mucous degeneration (Plate III, B). In other cysts the material stained a deep pink, granular or vacuolated in appearance (Plate I, B). In this material, especially towards the edge, many cholesterol crystals together with groups of cells and isolated cells resembling those

undergoing fatty metamorphosis were noted; also a few nuclei, which stained a pale blue, the cell-body apparently having disintegrated.

In addition to the above cysts, a few openings similar to gland ducts were seen. One opening branched twice, and these branches also divided, resembling a compound tubular gland (Plate V, A). This duct-like arrangement existed in several serial sections, demonstrating that the lumen was of considerable size. The walls, which were sharp and clean-cut in outline, consisted in every case of a number of layers of epithelial cells, not like the ragged walls of the cysts described above.

The Skin covering the Tumor.—The epithelial layers were normal, except that at the summit of the tumor the papillæ of the true skin had all been much shortened and the spaces between the papillæ widened. Between the epithelial layers of the skin and the epithelium of the tumor there was a band of connective tissue, the pars papillaris and pars reticularis of the true skin.

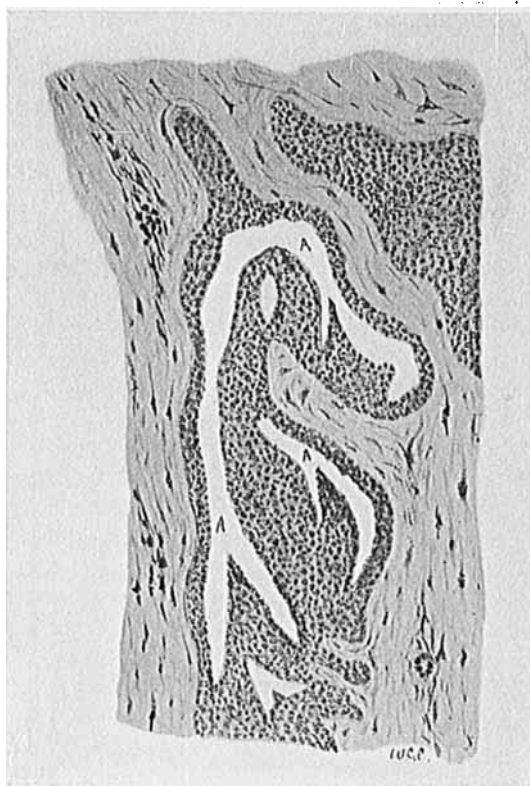
Diagnosis of Present Case.—An epithelial cystic growth of this nature, with cells undergoing fatty changes, could have originated from any one of the following: (A) The glands in the wall of a dermoid cyst; (B) the epithelium of an inclusion cyst; (C) a supernumerary mammary gland; (D) the sweat-glands; or (E) the sebaceous glands of the normal skin.

(A) The first of the above possibilities is ruled out by the fact that no hair-follicles or other remains of the wall of a dermoid cyst existed, such as stratified squamous epithelium, spine, or prickle cells.

(B) The presence of compound gland ducts, the absence of stratified epithelium, and the large size of the epithelial cells, discredit the growth as having originated from the wall of an inclusion or epidermoid cyst; also, there are no glands found in the walls of inclusion cysts from which an adenoma might spring.

(C) The tumor could not have originated from a supernumerary mammary gland, since it did not have any of the characteristics of such a growth.

PLATE V.



(D) The fourth possibility, that the tumor originated from a sweat-gland, can be easily ruled out because in the present tumor the epithelial cell-body did not stain as deeply as sudoriparous cells; and the gland-ducts were compound and thick walled, whereas in tumors growing from sweat-glands the ducts do not usually branch and their walls are lined by only one or two layers of cells. Klauber¹ has recently described sweat-gland adenomata in which there were many small cysts and gland tubules, whose walls consisted of a thin layer of epithelial cells.

(E) Therefore, having eliminated the four preceding possibilities, the existence of a pathological development of the infundibula of sebaceous glands remains for consideration. In this connection, attention is called to the deep situation of the tumor and its apparent separation from the skin; to the complex alveolar arrangement; to the formation of compound ducts; to the sparseness of ducts in a given section; to the formation of sebaceous material in one of the cysts, probably from cells in the wall, more like cells found in the normal sebaceous glands undergoing fatty metamorphosis; to the absence of laminated material such as is found in cysts formed from cells, which ultimately would have produced pavement or stratified squamous epithelium; and to the large size of the cells in the alveoli similar to sebaceous cells, and not like cells of the epidermis, except the basal cells, which are similar in character and continuous with the germ or basal cells of sebaceous glands.

RÉSUMÉ OF THE LITERATURE OF TRUE ADENOMATA OF SEBACEOUS GLANDS.

Bock,² in 1880, gave an exceedingly good description of the condition. In speaking of adenomata of sebaceous glands, he said the literature was very scanty. He mentioned Schmidt's *Jahrbücher*, in which there is an article by Porta³ on tumors of sebaceous follicles. The date of this article is 1856; in it there is given a list and the situation of 384 tumors; 238 were cystic, twenty-six of them being sebaceous. No detailed

microscopic description was given. Bock also mentions Förster's "Handbuch der Allgemeine pathologische Anatomie," S. 179, as referring to hypertrophy of sweat and sebaceous glands in contradistinction to that of sebaceous gland tumors. Bock further quotes Rindfleisch, "Lehrbuch der pathologische Geweblehre," S. 288, as describing a case of pure hypertrophy of a sebaceous gland tumor which had a broad base covered by the hairy scalp. The tumor was the size of a pigeon's egg, and its structure resembled that of a mammary gland. Birch Hirschfeld is also mentioned as citing the preceding case, and considers the true hypertrophy of sebaceous glands as probably very rare.

Bock's own specimen was eight centimetres in length, six centimetres in breadth, and three and five-tenths centimetres in height. Cut sections showed many epithelial alveoli separated by connective-tissue bands. The skin was apparently normal, except in places the papillæ were somewhat elongated. The lobules of the tumor had diameters of from one to six millimetres and were either round or elongated. In the gland substance were openings, microscopic in size, some cut squarely across, others obliquely. In places he found the centre of the lobules filled with cells undergoing fatty degeneration, with fat drops and granular masses. Towards the centre of the alveoli the cells were larger, appearing always epidermic in character and dimmed with fat; these changes in the cells were the causes of the construction of fat drops and granular masses in many acini. The sweat-glands were normal and regular. He gives a drawing showing the general topography of the epithelial alveoli with the central openings and with the normal condition of the skin covering the tumor; also a drawing of one-half of an alveolus, showing the outside cells clear and regular in arrangement, with fat drops increasing in number towards the centre of the alveolus, which is filled with a homogeneous mass.

Eve,⁴ in 1881, gave a good description of a partly cystic and partly adenomatous tumor which had become calcified. His plate certainly shows the lobules of an adenoma. The tumor measured one and one-quarter by one-half inches. It was seen to consist of columns, made up of epithelial cells, which presented every variety of size, from minute round masses of cells, one-fortieth of an inch in diameter, to large columns or cylinders one-half to three-quarters of an inch in diameter, having the appearance of alveoli in transverse section. In the sections the alveoli were cut across in various directions and were round or oval; the smaller columns were in places irregular, tortuous, branched, and occasionally uniting. The cells were small, round or oval, closely packed together without intercellular substance. Occupying a position near the centre of many

of the larger columns, and in a few instances of the smaller, unstained granular masses were observed, which were probably the seats of the calcareous matter. This material was found, on further examination, to consist largely of fatty matter containing crystals of cholesterin, and may be regarded as an attempt at the formation of sebum by the gland tissue. Eve thinks it may be regarded as an adenoma associated with the sebaceous glands.

Krauss,⁵ in 1884, in an article concerning giant cells in epithelial growths, mentions an adenoma of sebaceous glands, a tumor, 2.9 centimetres by 2.5 by 1.7 centimetres, on the left arm of a man twenty years of age. This fairly solid tumor was soft and contained a doughy mass in the centre. The skin was quite thin and separate from the growth, a firm connective-tissue capsule enclosing it. The epithelium was arranged in lobules, round or oval in shape, at times tubular. The centres of the lobules and tubules were filled with a firm necrotic mass from degenerating cells. A cut is given showing several alveoli with centres filled with the necrotic masses. He mentions sweat-glands as if they had no connection with the tumor.

Poncet,⁶ in 1890, described a case of a man of fifty-three years of age, who, for thirty years or more, had over sixty tumors on his head alone. A cut is given showing a man's head covered with large-sized, closely set tumors; a very prominent one is seen on his forehead. Microscopic examination of one of these tumors by Band showed it to be made up of round lobules separated by connective-tissue bands. The lobules are composed of epithelial cells. The cells have the same characteristics as young sebaceous gland cells. The peripheral cells of the lobules are in regular rows. In the centre of most of the lobules there is an unstained part, light gray or colorless; this part looks like a sebaceous mass. He concludes that it is a tumor made up of epithelial cells similar to sebaceous gland cells.

Jarisch⁷ gives a few cases of skin tumors, with many good cuts, and also reviews the literature of sebaceous adenoma.

Richard Barlow,⁸ in 1895, reviewed the whole subject thoroughly. He describes a case of multiple tumors of the scalp, of six years' duration, in a person sixty years of age, and calls it a case of adenomata of the sebaceous glands. He speaks of the definition of adenoma, and quotes Förster, Cohnheim, Ziegler, and others. He also speaks of the different types of lesions of these glands. In conclusion, he says an adenoma may occur in sebaceous glands, may become calcified, and also may become cancerous. He gives several plates of adenoma of sebaceous glands of the scalp.

Curtis and Lambret,⁹ in 1900, review the subject up to

date, and describe a large tumor of eight years' growth, which clinically was thought to be malignant; histologically it was thought to be a simple adenoma of the sebaceous glands and similar to Bock's, Monti's, and others.

Borst¹⁰ in his book on tumors shows a picture of a sebaceous adenoma which was made up of lobules of epithelial cells separated by bands of connective tissue. The lobules are very irregular in shape, their centres occupied by masses of sebaceous material. He says that a pure adenoma of sebaceous glands, either a solitary, nodular, fleshy, or sometimes ulcerated, encapsulated tumor, may exist, which is made up of epithelial lobules, the centres of which are filled with fatty masses. The connective tissue and vessel walls may undergo hyaline degeneration; also, in an adenoma the peripheral germ cell layers, which shut in or enclose the epithelial cells of the follicle, spread out, while the old central layers of cells are mostly overwhelmed by fat infiltration, and, in consequence, they are not of a typical form, so that the enclosed fat mass in the centre grows from the rupture of these cell-bodies.

Krompecher,¹¹ in 1903, mentions the relation that may exist between the basal cells of hair-follicles, or of sweat or sebaceous glands, and flat-celled cancers, also the similarity of structure of sebaceous glands to breast glands; and gives a diagram of different types of sebaceous gland hypertrophy, showing how different types of tumors may develop from the different epithelial layers of the skin.

Levings,¹² in 1903, speaks of adenomata of sebaceous and sudoriparous glands. "These growths are of rare occurrence. When taking origin from the sebaceous glands they are closely adherent to the skin, are round or slightly lobulated, elastic, and reasonably hard growths. They are made up of an aggregation of alveoli, and are to be differentiated from the ordinary wen and from the tumors which are entirely subcutaneous. In size they are usually small, often not exceeding that of a hickory-nut, but in exceptional cases they have become quite large."

Ribbert¹³ mentions adenoma of the sebaceous glands and speaks of Barlow's article.

*Unna's*¹⁴ *Review of the Relation of Adenoma and Hyperplasia of the Sebaceous Glands.*—Under hypertrophy of the sebaceous glands, Unna says that simple hypertrophy of the sebaceous glands appears partly as an accompaniment of other processes, partly as an independent tumor. The independent tumors are rare; much more frequent is the more or less diffuse hypertrophy of the glands, which chiefly accompanies the chronic forms and results of seborrhœic catarrh, especially of the nose and the middle of the forehead.

Adenoma of sebaceous glands, Unna calls "Steatadenoma." "The definition of adenoma can certainly not be applied, where the sebaceous gland epithelium produces solid bodies, which grow into solid epithelial masses or epithelial cords; we have, then, some form of acanthoma proceeding from the sebaceous gland. The participation of the sebaceous gland in an epithelial growth, proceeding from the follicle or the surface epithelium, is a very frequent occurrence accompanying the most varied inflammatory and hypertrophic conditions." "It thus appears as if we must abandon the definition of steatadenoma in the strict sense of the word, since the benignant tumors of the sebaceous glands are either hypertrophies or acanthomata of the sebaceous glands. But there might also be tumors occupying a median position between the condition just mentioned, in that, for example, solid bodies first come from the sebaceous epithelium, which, after they have developed in a tumor-like fashion, again recall their point of origin by fatty degeneration of their cells. Then we would have a growth in a new direction agreeing with the definition of an adenoma, if we retain it, and at the same time the proof that the cells of the growth had not lost their character as sebaceous cells during growth. If no such tumors were to be found, then it would be better to abandon altogether the term 'adenoma of the sebaceous glands;' but there is the case recorded by Bock which agrees with the following strict definition of steatadenoma, benign tumor-like growths of irregular formation proceeding from the epithelium of the sebaceous glands, in whose outgrowths fatty but no colloid metamor-

phosis takes place." Unna quotes from Bock, and says, "The development of the glandular lobules took place from below upward. Bock founded the diagnosis steatadenoma on the triple recognition, first, of the normal behavior of the sweat-glands; second, of the absence of cancerous processes, and, third, of the presence of acini, which in their development, evolution, fatty degeneration, and calcification corresponded with sebaceous glands." In conclusion, he says that one must admit that this origin would have been still clearer, if, at the more recent parts of the growth, a true formation of sebaceous glands had been recognized, with a reticular spongy character of the cell protoplasm, as in the fatty changes in true sebaceous cells.

RÉSUMÉ OF THE LITERATURE OF HYPERPLASIA OF SEBACEOUS GLANDS, EITHER ALONE OR SECONDARY TO HYPERTROPHY OF THE SKIN.

Pringle,¹⁸ in 1890, reported a case of many small, indolent, firm, whitish, solid papules or little tumors of the face embedded in the skin, the largest the size of a small pea and near the nasolabial fold. When pricked with a pin, white sebaceous matter could be expressed. The superficial layers of epithelium along the whole section were rather thin; the rete showed excessive and irregular involution, dipping deeply into the subjacent derma. The chief pathological changes were found in the corium; its upper papillary layer was enormously hypertrophied, but it was in the deeper layers that the essential lesions lay. They consisted of an enormous increase in number and complexity of the sebaceous glands. The gland epithelium was everywhere well formed, the acini at no spot exhibiting retrogressive changes. A good microphotograph was given; also a chrome lithograph of a girl's face studded around the nose and on the cheeks below the eyes with small flat tumors. He cites Balzer's¹⁹ cases, and agrees with him in using the term "adenomata."

Caspary,²⁰ who followed Pringle in 1891 with a very similar case, described a girl's face covered with small nodules. He showed a good lithograph and microscopic sections of the conditions. He gave Pringle's as the sixth and his as the seventh case on record.

Pollitzer,²¹ in 1893, described and gave a clear photograph of a group of thirty small adenomata, as he calls them, on the forehead of a man twenty-five years of age, in whom the condition had lasted six years. Each nodule was as large as a medium-sized barley-corn. Two were cystic and sebaceous matter could be expressed from almost all. The microscopic examination of excised specimens showed that almost the entire specimen was made up of sebaceous gland tissue, which had preserved the lobulated

arrangement of the normal gland. The resemblance in both the appearance of the cells and their arrangement to normal sebaceous glands was so close that he suspected it to be hypertrophy of the gland. Actual measurement of the individual gland cell showed no increase in size beyond the normal, and there were far more than the normal number of lobules. The condition, then, could only be called adenoma. He gives a cut, and says, "Two club-shaped processes of epithelium may be seen shooting out from the side of the root-sheath of a hair, exactly like the buds from which the glands are formed in the embryo. Near the end of one of them a small island of epithelial cells appears as if cut off from the growing shoot. Such an isolated group of cells would, as they underwent their physiological fatty degeneration, necessarily give rise to a sebaceous cyst. Sweat-glands appear normal and far below the tumor." He said there were scarcely twenty cases of this rare disease observed, and this was the first and only one in America. He mentioned Crocker's, Jameson's, and Caspary's cases.

Unna says that if any one attempted to apply the term adenoma to peculiar forms of simple sebaceous hypertrophy in such cases as those of Pringle and Caspary, it would be impossible to draw the line, and we should have to call every enlargement of the sebaceous glands adenoma.

Pezzoli,¹⁹ in 1900, described a very similar condition, and mentioned that Balzer and Ménétrier were the first to describe it in 1885. He gave a case of a great number of very small discrete tumors on the face of a young girl, showing a picture of the same, also a cut of a microscopic section.

Walther Pick,²⁰ in 1901, described with great care and detail a diffuse mass of small cystic skin tumors on the face of a man suffering from acne rosacea. The cysts were filled with a homogeneous material, and some of the cells were degenerating; also, some of the cell-bodies were much swollen, and at times fine protoplasmic scaffolding was seen which is found in normal sebaceous gland cells. The nature of the degeneration he attempted to prove by orcein stain and orange tannin. In normal sebaceous gland ducts, the dye stained the material a light yellow, and the cyst contents the same color. He also gave several very good lithographs of a diffuse hypertrophy or adenomatous condition of the sebaceous gland and hypertrophy of the skin, with no real tumor formation.

SUMMARY.

It is seen from a consideration of the cases cited by Bock and others, that, although denied by some observers, true adenomata of the sebaceous glands, without associated lesions of the skin, do exist, and that these adenomata undergo fatty metamorphosis with a formation of cysts. Tumors of this sort are rare, large ones especially so. On the other hand, adenoma, or an hyperplastic condition of the gland, secondary to or together with hypertrophy of the skin, is not so uncommon.

True adenomata of the sebaceous glands may become calcified or carcinomatous. The stroma of the tumor may undergo hyaline degeneration. Giant cells may occur in them.

The epithelial cells may undergo mucous degeneration and form cysts similar to those derived from the cell undergoing fat metamorphosis.

It has been shown that the tumor which is the subject of this paper is neither a dermoid cyst nor a simple inclusion cyst, nor is it derived from a supernumerary mammary gland, or the sweat-glands. It would therefore appear that the growth is a true adenoma starting from the infundibula of the sebaceous glands and retaining the type of the secreting portion. It thus has all the characteristics of a steatadenoma or adenoma of the sebaceous glands; namely, the presence of acini, which in their development, evolution, fatty metamorphosis, and calcification correspond to sebaceous glands.

I am indebted to Professor T. M. Prudden, Dr. John H. Larkin, and Dr. Charles Norris for many suggestions in connection with this article.

BIBLIOGRAPHY.

- ¹ Klauber. *Beiträge zur klinischen Chirurgie*, Band xli, S. 311.
- ² Bock. *Virchow's Arch.*, Band lxxxi, S. 503.
- ³ Porta. *Schmidt's Jahrbuch*, Band xcvi, S. 127.
- ⁴ Eve. *Transactions of the Pathological Society*, London, Vol. xxxiii, p. 335.
- ⁵ Krauss. *Virch. Arch.*, Band xcv, S. 249.
- ⁶ Poncet. *Revue de Chirurgie*, 1890, p. 244.

- ¹ Jarisch. Arch. f. Dermat. u. Syph., Band xxviii, S. 163.
- ² Barlow. Deut. Arch. f. klin. Med., Band iv, 61.
- ³ Curtis and Lambret. Revue de Chirurgie, Vol. xxii, p. 147.
- ¹⁰ Borst. Geschwulstlehre, Band ii, S. 577.
- ¹¹ Krompecher. Der Bazalzellenkrebs.
- ¹² Levings. The Ætiology, Pathology, Diagnosis, and Treatment of Tumors, p. 405.
- ¹³ Ribbert. Geschwulstlehre, S. 384.
- ¹⁴ Unna. The Histopathology of the Diseases of the Skin, p. 814.
- ¹⁵ Pringle. British Journal of Dermatology, 1890, Vol. ii, p. 1.
- ¹⁶ Balzer et Ménétrier. Arch. de Physiologie, 1885, p. 564.
- ¹⁷ Caspary. Arch. f. Derm. u. Syph., Band xxiii, S. 371.
- ¹⁸ Pollitzer. Journal of Cutaneous and Genito-urinary Diseases, 1893, Vol. ii, p. 475.
- ¹⁹ Pezzoli. Arch. f. Derm. u. Syph., Band liv, S. 193.
- ²⁰ Pick. Arch. f. Derm. u. Syph., Band lviii.